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AIDS and a Risk-Based Model 2

by Stirling A. Colgate, E. Ann Stanley, James M. Hyman, Clifford R. Qualls, and Scott P. Layne

A model that assumes people choose partners of similar sexual activity reproduces the observed cubic growth in AIDS cases, whereas most models predict exponential growth. A general distribution of sexual activity along with biased mixing are identified as the factors driving the epidemic from the highest to lower and lower risk groups.

Mathematical Formalism
by James M. Hyman and E. Ann Stanley

Numerical Results of the Risk-Based Model
by James M. Hyman, E. Ann Stanley, and Stirling A. Colgate

The Seeding Wave
by Stirling A. Colgate and James M. Hyman

Genealogy and Diversification of the AIDS Virus 40

by Gerald L. Myers, C. Randal Linder, and Kersti A. MacInnes

Comparison of the DNA sequences of HIV from various AIDS victims reveals a genealogy for the virus that agrees with the epidemiology of the disease.

Viruses and Their Lifestyles

An HIV Database

AIDS Viruses of Animals and Man: Nonliving Parasites of the Immune System 54

by Peter Nara of the National Cancer Institute

A class of "slow" viruses has evolved a full bag of tricks allowing them to use the immune cells of animals and man as a comfortable ecological niche and then to outsmart vaccines designed to evict them from that niche.

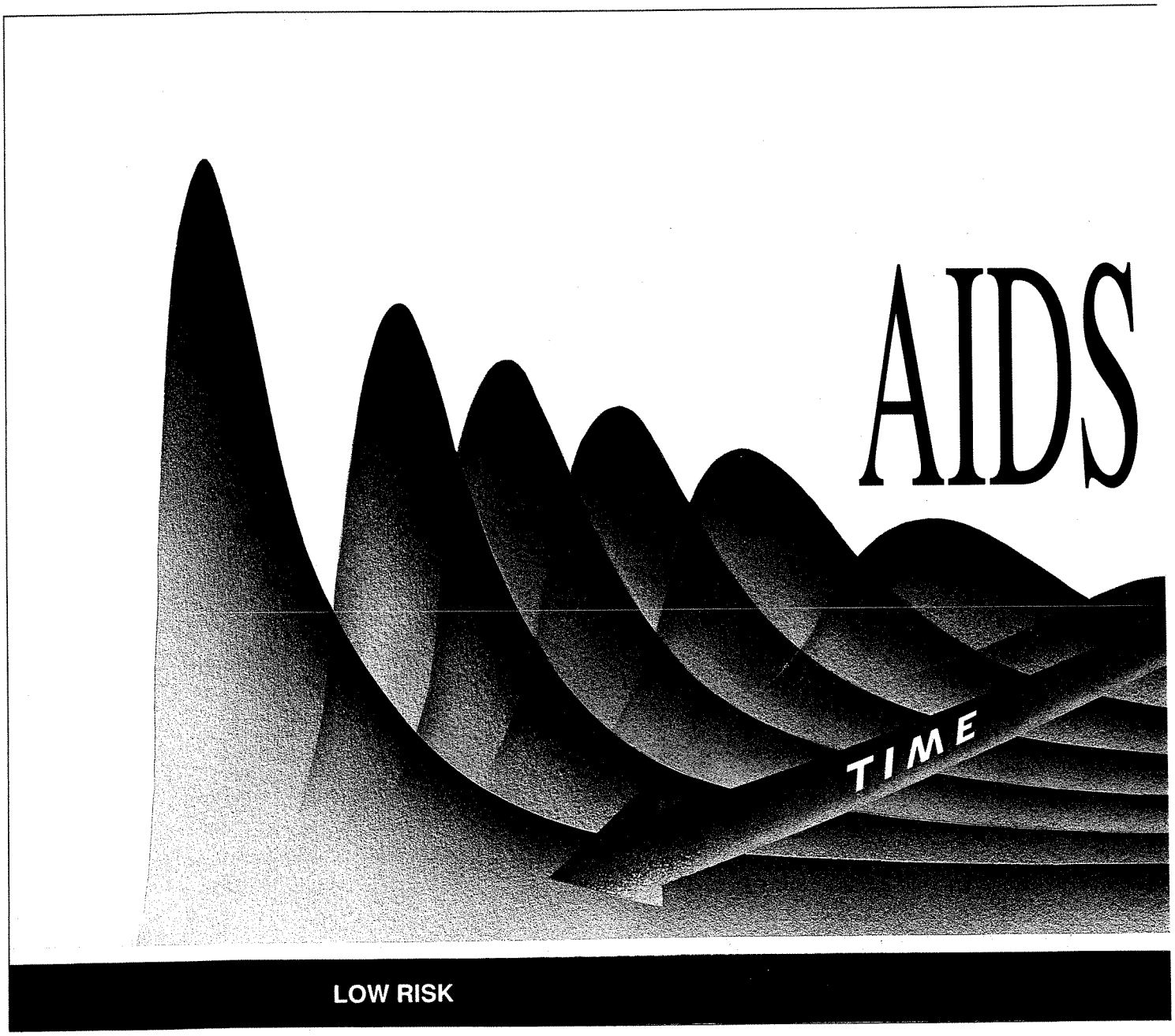
The Search for Protective Host Responses

The Kinetics of HIV Infectivity 90

by Scott P. Layne, Micah Dembo, and John L. Spouge

A first attempt to model the kinetics of viral infectivity in culture should help standardize laboratory experiments and help evaluate various treatment strategies for AIDS.

Mathematical Considerations



The biased-mixing risk-based model predicts that HIV infection spreads through the population from high-risk (red) to low-risk (blue) groups. The graph shows number of people infected (vertical scale) versus risk (left to right) versus time (back to front). As time increases, the peaks occur at lower and lower values of risk behavior. Also, they increase in height because there are many more people in low-risk than in high-risk groups.

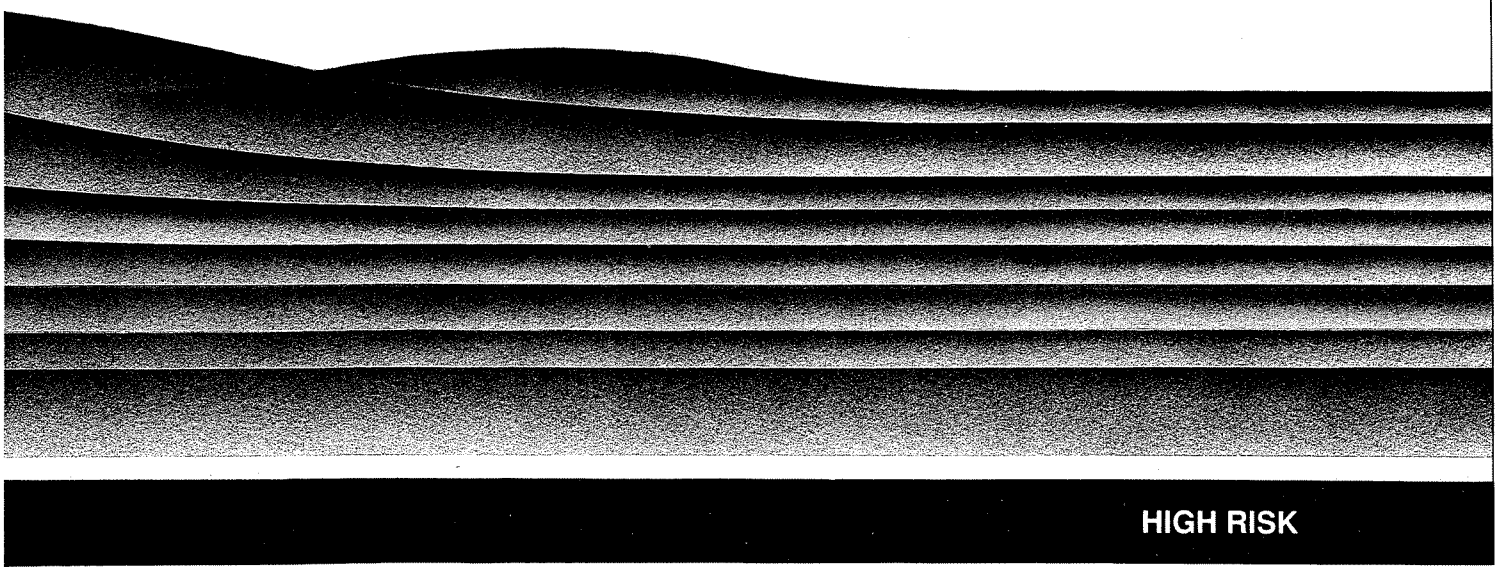
The threat of AIDS looms ominously over society. It has already devastated the male-homosexual population and is spreading rapidly among intravenous-drug users, through sexual contact to their partners and through perinatal contact to their children. Although many promising therapies are on the horizon, it appears unlikely that a definitive cure or preventive vaccine will ever be developed. Also, we don't know where this lethal disease will spread next and whether it will reach epidemic proportions among the bulk of our population.

In an effort to make a quantitative assessment of the threat, we adopted the philosophy that to predict the future we need to understand the past. How has the number of AIDS cases grown over time? How has the number grown among various subgroups of the population? What risk behavior is correlated with becoming infected? How does the long and variable time between infection and appearance of symptoms affect the spread of the disease? Can the known data be used to make a plausible model that agrees with the history of the epidemic to date?

We began our effort by looking at the most reliable data on the course of the epidemic—those compiled by the Centers for Disease Control (CDC) on the total number of AIDS cases in the United States as a function of time.

and a risk-based model

by Stirling A. Colgate, E. Ann Stanley, James M. Hyman, Clifford R. Qualls and Scott P. Layne



Airbrush art by David Delano

Because the United States has a large number of AIDS cases and a legal requirement for reporting them, the CDC data are the most statistically significant available.

Analysis of the United States data revealed two surprising facts. First, the number of cases has not grown exponentially with time, but rather cubically with time, or as t^3. The difference may not appear significant until one realizes that previous epidemiological models for the spread of diseases predict exponential growth during the early phases of an epidemic, and further, most epidemics so far studied have followed that pattern. The second surprise came when the data were broken down into subgroups by race and sex or sexual preference. Again the number of cases in each subgroup grew as t^3, and further, the cubic growth for each group appeared to start at nearly the same time.

The model we present here was developed to explain the cubic growth of AIDS cases in the United States. It builds on the fact that the level of "risky" behavior—in particular the sexual behavior that puts one at risk of contracting the AIDS virus—varies among the population according to a distribution that we speculate may be universal for all populations. Thus it is called a risk-based model. It also depends on another assumption about human behavior, namely, that people

with similar risk behavior tend to mix, or interact, primarily among themselves (biased mixing) rather than randomly with everyone (homogeneous mixing). The details of our risk-based, biased-mixing model form a logical, coherent framework for interpreting the currently available data for the United States, but before we launch into details we want to emphasize one critical insight.

Since the growth in number of AIDS cases is cubic, the doubling time for the epidemic (the time for the number of cases to double) is continuously increasing. By contrast, if the growth were exponential, the doubling time would remain constant. In the framework of standard epidemiological models, the observed lengthening of the doubling time for AIDS (and hence its decreasing relative growth rate) might be attributed to changes in people's sexual behavior as a result of learning about AIDS. That interpretation has been promulgated in the press and has fostered complacency about the efficacy of education. Unfortunately, it is false because the long incubation time from infection to AIDS means that the effects of learning could not have been seen in the data until very recently.

The people who developed AIDS in the early to mid 1980s were infected with the virus that causes AIDS (the human immunodeficiency virus, or HIV) in the late 1970s and early 1980s, long before learning could have affected a major fraction of the male-homosexual population. So behavior changes, if any, could not have been nearly enough to give cubic growth of AIDS in the late 1970s and early 1980s. Thus the impact of learning cannot explain the observed cubic growth. Another possibility to consider is that the combined effect (or convolution) of an exponential growth in HIV infections and a highly variable time for conversion from infection to AIDS yields a power law. After an initial transient, however, an exponential convoluted with any bounded conversion function is still an exponential, not a power law. Moreover, it is unlikely that the initial transient would have the long, clearly defined cubic behavior seen in the data.

We have looked with considerable diligence for possible causes of cubic growth other than behavioral changes due to learning. We have concluded that the risk-based, biased-mixing model presented here best fits the observations. Our model is an extension of an earlier risk-based model of May and Anderson. They assumed homogeneous rather than biased mixing of the susceptible population and so predicted an exponential for the early stages of the epidemic. We have drawn much from their work, but it was the contradiction between the theoretically nearly inevitable early exponential growth and the observed cubic growth that led us to the following biased-mixing model. We also realized that random mixing is sociologically unrealistic.

The general mathematical formalism for our model is presented in "Mathematical Formalism for the Risk-Based Model of AIDS." Numerical solutions for different assumptions about population mixing and variability of infectiousness are presented in "Numerical Results of the Risk-Based Model." Here we will present an intuitive and simplified version of the model that emphasizes the main features leading to cubic growth, the quantitative predictions of the model, and the questions about human behavior and HIV transmission that must be answered before we can determine whether the patterns we have identified for the past will continue in the future.

Cubic Growth of AIDS

The CDC data on cumulative number of AIDS cases in the United States between mid 1982 and early 1987 are shown in Fig. 1. Data for times prior to 1982.5 are not shown because they are statistically unreliable. Data collected since 1987.25 are also not shown because the surveillance definition of AIDS was changed in 1987. The effects of that change on reporting delays and/or on the cumulative number of AIDS cases have not been fully determined, but preliminary analysis suggests that

GROWTH OF AIDS IN THE U.S.

Fig. 1. Cumulative number of AIDS cases reported to the Centers for Disease Control through mid-1987. Data for times before mid-1982 are statistically unreliable and therefore not shown. More recent data have yet to be adjusted for the CDC's change in the definition of AIDS in May 1987.

CUBIC GROWTH OF AIDS

Fig. 2. The near linearity of this cube-root plot of the data shown in Fig. 1 indicates that the cumulative number of AIDS cases can be well represented by a cubic polynomial. We found that the best cubic fit is $A(t) = 174.6(t - 1981.2)^3 + 340$, where $A(t)$ is the cumulative number of AIDS cases and t is the yearly date. That fit reproduces the data to within 2 per cent.

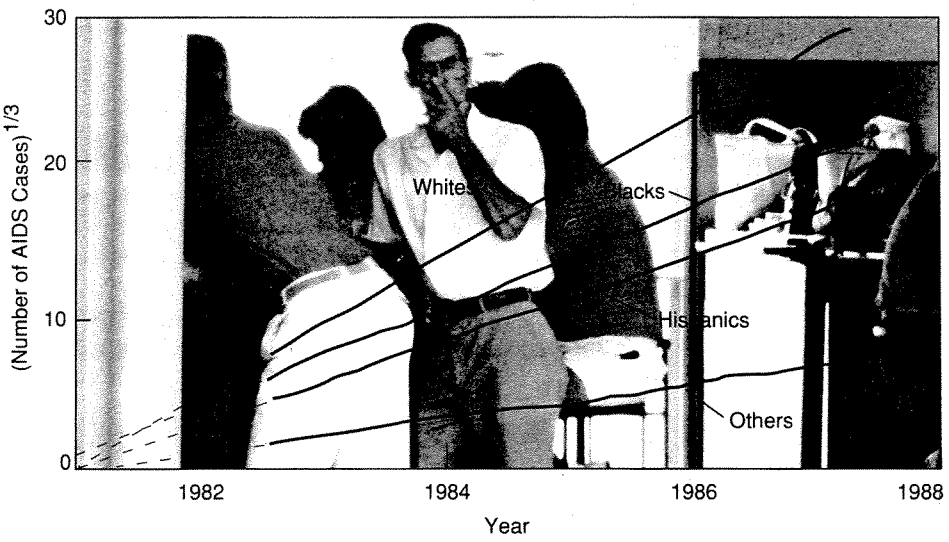
AIDS cases have continued to increase in a regular manner. The best fit to the data in Fig. 1 is the cubic function

$$A = 174.6(t_y - 1981.2)^3 + 340, \quad (1)$$

where A is the cumulative number of AIDS cases and t_y is the date in years. All the constants, including the date 1981.2, were determined by the statistical analysis. The cubic fit reproduces the data between 1982.5 and 1987.25 to within an accuracy of 2 per cent.

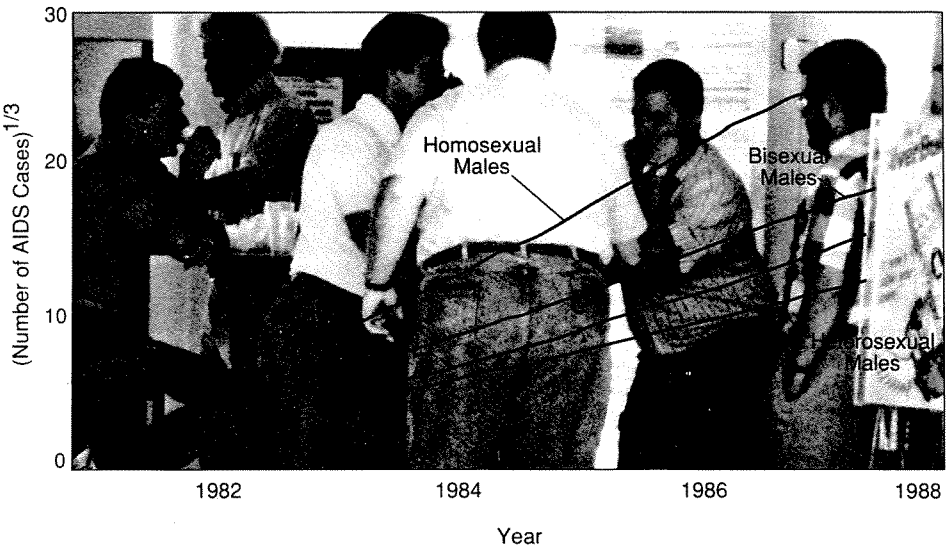
BREAKDOWN OF AIDS CASES BY RACE

Fig. 3. Plots of the cube root of the cumulative number of AIDS cases among homosexual, bisexual, and heterosexual males and among females are all nearly straight lines, indicating that AIDS has grown cubically in each group. Further, extrapolation of the curves (dashed lines) indicates that cubic growth began in all groups at approximately the same time that it began in the population as a whole. (Intravenous drug users have not been removed from the subgroups and the heterosexual-male subgroup includes cases of transfusion-related AIDS among juvenile males.)



BREAKDOWN OF AIDS CASES BY SEX AND SEXUAL PREFERENCE

Fig. 4. Plots of the cube root of the cumulative number of AIDS cases among whites, blacks, Hispanics, and other racial groups again indicate cubic growth of AIDS beginning about 1981. Breakdowns of the data by geographic categories also show cubic growth.



To show the cubic growth more clearly we plot the cube root of the total number of AIDS cases in Fig. 2 and see surprisingly small deviations from a straight line, of the order a few per cent for $t_y \geq 1982.5$. Hence, if we measure time t from 1981.2 and neglect the small error, then

$$A = A_0 + A_1 t^3, \quad \text{for} \quad t > 1.3 \ \text{years}, \tag{2}$$

where $A_0 = 340$ and $A_1 = 174.6$. Thus, after an initial transient, AIDS cases grow as the cube of time.

Breakdowns of the data by sex or sexual preference (Fig. 3) and race (Fig. 4) again show the same form of cubic growth for each subgroup. This is surprising, since the fact that the sum of all the data is cubic requires that the separate cubics be synchronized in time, in this case to within less than six months. In addition to presenting our model for cubic growth, we will discuss a possible seeding process for the initial cases of AIDS (see "The Seeding Wave") that is consistent with both the assumptions of our model and the synchronization of cubic growth in various subgroups.

Currently (third quarter of 1988), the CDC reported a cumulative total of 74,904 AIDS cases under their expanded mid-1987 surveillance definition. Of those about 14 per cent fell under the new categories added in mid-1987. More difficult to determine are the effects of delays between diagnosis and reporting to the CDC caused by the redefinition. The median reporting delay prior to the redefinition was about 3 months, and adjustments made for those delays have visible effects 36 months into the past on a graph such as the graph shown in Fig. 1. After the redefinition in mid-1987, the median reporting delay lengthened to about two years, and the reporting situation is still in transition. Consequently, we must await further data before we can model the effects of the transient caused by the redefinition and determine whether or not cubic growth has continued to the present. Nevertheless, we can say with certainty that the growth in AIDS cases is still polynomial of degree less than 4.

Expected Exponential Growth

We start by showing that the initial growth of AIDS (or of any infectious disease) would be exponential provided the population was homogeneous and did not change its behavior. We assume AIDS is the long-term result of infection by HIV and derive an equation for the rate of growth in the number of infected persons. Let I be the number of persons infected at time t in a population of size N. Assume that α, the rate at which an infected person transmits the AIDS virus to others, does not vary with time nor from person to person. Then during the time interval dt the I infected persons in the population would infect αI persons. But the fraction I/N of those αI persons are already infected, and so the number of additional persons infected during dt is $\alpha I - \alpha I(I/N)$; that is,

$$\frac{dI}{dt} = \alpha I \left(1 - \frac{I}{N}\right). \tag{3}$$

Equation 3 is called a logistic equation (or an equation of mass action) and is the basic equation of epidemiology. During the initial phases of the epidemic, $1 - \frac{I}{N}$ is approximately 1, and we can approximate Eq. 3 by

$$dI/dt = \alpha I. \tag{4}$$

Equation 4 has the exponential solution

$$I = I_1 e^{\alpha t}, \tag{5}$$

where I_1 is the number infected at $t = 0$.

Exponential growth is characteristic of the initial phase of many epidemics and is a solution of many current AIDS models. Note that exponential growth implies a constant relative growth rate:

$$\text{relative growth rate} \equiv \frac{dI/dt}{I} = \alpha. \tag{6}$$

The number infected will continue to grow exponentially until the fraction infected is no longer small compared to unity. The population is then said to be approaching saturation, and the relative growth rate decreases. However, we have observed that even the first few thousand AIDS cases show cubic, not exponential, growth, so saturation of the population cannot be the explanation for the decrease in the relative growth rate.

What Makes a Power Law? Suppose now that the relative growth rate α is not constant in time but instead decreases inversely with time:

$$\alpha = \frac{m}{t}, \tag{7}$$

where m is a constant. Then Eq. 4 becomes

$$\frac{dI}{dt} = m\frac{I}{t}. \tag{8}$$

Equation 8 has a power-law solution, namely,

$$I = I_1 t^m; \tag{9}$$

that is, the number infected grows as the mth power of time. Moreover, since the doubling time t_d is inversely proportional to the relative growth rate m/t, t_d increases proportionally to t. In particular, $t_d = (\sqrt[m]{2} - 1)t$. The growth of AIDS is cubic, so $m = 3$ and $t_d = (\sqrt[3]{2} - 1)t \approx 0.26t$. The observed doubling time for the AIDS epidemic has increased linearly from less than 0.5 year to the current value of more than 2 years. That change in doubling time and relative growth rate (by more than a factor of 4) is dramatically different from the constant doubling time characteristic of exponential growth.

A Risk-Based Model

Any model for the spread of an infectious disease must take into account the mechanism of its transmission, the pattern of mixing among the population, and the infectiousness, or probability of transmission per contact. The primary mechanisms for transmitting the AIDS virus are sexual contact and sharing of intravenous needles among drug users. Since little is known about needle-sharing habits, we concentrate on transmission through sexual contact. Here we build on data from the homosexual and heterosexual community. The relative growth rate of infection α can be approximated as the product of three factors: the infectiousness i, or probability of infection per sexual contact with an infected person; the average number of sexual contacts per partner c; and the average number of new partners per time interval p. That is,

$$\alpha \approx icp. \tag{10}$$

Each of the factors in Eq. 10 can be a complicated function. For example, data suggest that infectiousness i is, on average, between 0.01 and 0.001 and that it varies with time since infection and, perhaps, from individual to individual (more about that later). The new-partner rate and the average number of contacts per partner certainly vary among the population and may depend on age, place of residence, race, personal history, and more. The general model presented in "Mathematical Formalism for the Risk-Based Model of AIDS" allows for some of these variations, but here we pick out the simplest features that lead to cubic growth.

The first crucial assumption of the risk-based model is that the susceptible population is divided into groups according to level of engaging in behavior that can lead to infection. The risk behavior most often correlated with HIV infection in the male-homosexual population (as suggested by the early work of the CDC) is frequent change of sexual partner, which we quantify as new-partner rate. The other behavior we consider is frequency of sexual contact (which is equal to the product cp in Eq. 10). Both sexual contact and some new partners are necessary to cause the epidemic.

If our model is to agree with observation, we must assume that the members of each risk group (whether the risk be new-partner rate or sexual-contact frequency) interact primarily, but not exclusively, among themselves; in other words, the mixing among the population as a whole is biased. We also assume that mixing within each risk group is homogeneous and that the relative growth rate α is proportional to the risk behavior r,

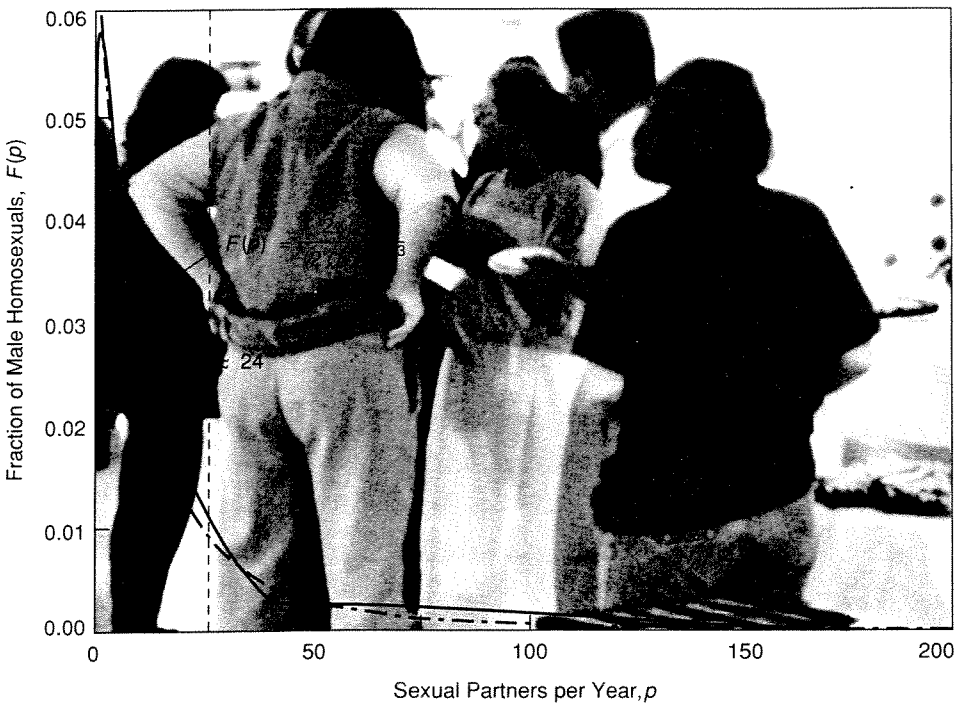
$$\alpha = \alpha' r, \tag{11}$$

so that infectiousness i is approximated as a constant.

Finally we assume (and justify below) that risk behavior is distributed among the high-risk groups as r^{-3}; that is, the number of people with risk behavior r, $N(r)$, is given by $N(r) \propto r^{-3}$. We believe that these assumptions are sufficient to explain the cubic growth of the AIDS epidemic. For the purposes of the model, it makes no difference what the risk behavior actually is—only that such a behavior exists and is distributed approximately as r^{-3}. However, because of past preconceptions and universal interest, we discuss the available data on the distribution of both new-partner rate and sexual-contact frequency. In doing so, we restrict ourselves primarily to cases of AIDS among homosexuals, which constitute roughly 65 per cent of the total number of cases. Our model can be applied to intravenous-drug users only when additional risk-behavior data are available.

Distribution of Risk Behavior

New-Partner Rate among Male Homosexuals. The best available data on new partner rate p come from studies of homosexual men. Although those data are usually presented in summary form (number with 20 to 40 partners in the past year, for example) and the sizes of the study samples tend to be small, all of the studies find similar distributions. The standard deviation σ is always larger than the mean $\langle p \rangle$, sometimes much larger. In other words, the population is not clustered about the mean but rather varies widely in its behavior. Moreover, a good fit to the data for



DISTRIBUTION OF NEW-PARTNER RATE

Fig. 5. A plot of $F(p)$, the fraction of a group of male homosexuals that had p sexual partners per year, versus p. Members of the group were attendees at London clinics for sexually transmitted diseases. (For more details about the data, see May and Anderson.) Also shown is our inverse-cubic fit to the data, $F(p) = 2\langle p \rangle^3/(p + \langle p \rangle)^3$, where $\langle p \rangle$ is the mean number of partners for the whole group.

p greater than a few partners per year is the distribution $p^{-\beta}$, where β is between 3 and 4. Figure 5 shows combined data from two studies of homosexual men attending London clinics for sexually transmitted diseases. Also shown is our cubic fit to the data $2\langle p\rangle^3/(\langle p\rangle + p)^3$. The two London studies are biased away from low-activity homosexual men; more randomly chosen samples tend to exhibit a $p^{-\beta}$ distribution at large p, but larger fractions of the samples lie at low p.

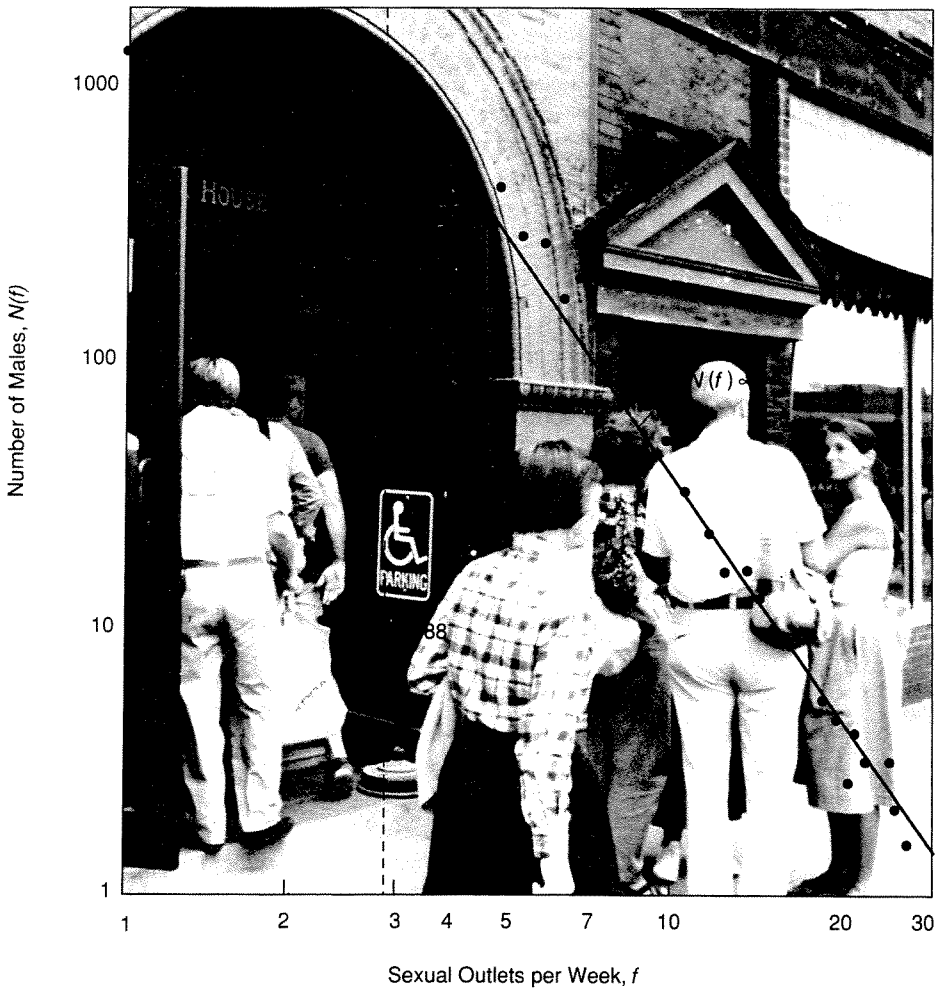
Either the published data are too crude (especially since the maximum value for the highest bin tends to be omitted) or the sample sizes are too small to distinguish between $\beta = 3$ and $\beta = 4$. In this paper we have chosen to use $\beta = 3$ to be consistent with the sexual-outlet frequency data of Kinsey, Pomeroy, and Martin (see below). The choice is important because in our model the value of β determines the growth rate of the epidemic (AIDS cases increase as t^{β}).

(One way to test the hypothesis that $\beta = 3$ for male homosexuals is to determine how the standard deviation σ of the distribution varies with sample size. If p is distributed as p^{-3}, then $\sigma/\langle p\rangle$ will increase as the sample size increases. By contrast, if p is distributed as p^{-4}, then $\sigma/\langle p\rangle$ will approach a limiting value of 4 as the sample size increases. Unfortunately, the data available are insufficient for us to apply this test.)

Sexual-Contact Frequency among Males. We now turn to the distribution of sexual-contact frequency. For that information we must rely on the data published in 1948 by Kinsey, Pomeroy, and Martin on sexual-outlet frequency among 11,467

DISTRIBUTION OF SEXUAL OUTLET FREQUENCY

Fig. 6. A plot of $N(f)$, the number of males among a large study group that had f sexual outlets per week, versus f. Also shown (solid line) is a distribution that fits the data well: $N(f)$ = constant for $f < \langle f\rangle$ (the mean sexual-outlet frequency) and $N(f) \propto f^{-3}$ for $f \geq \langle f\rangle$. The data are those of Kinsey, Pomeroy, and Martin for a group of 11,467 American males ranging in age from adolescence to thirty years.



American males ranging in age from adolescence to thirty years (Fig. 6). (The sexual outlets considered by Kinsey et al. include activities, such as masturbation, that are of little relevance to the spread of HIV infection. However, data more appropriate to our needs are not available.) We found that the Kinsey data could be well fit with a distribution similar to the distribution of new-partner rate among homosexual men. For values of sexual-outlet frequency f above the mean, the number of males at each f value, $N(f)$, is proportional to f^{-3}. The entire distribution is given by

$$\frac{N}{N_0} = \begin{cases} 1 & \text{if } f < \langle f \rangle \\ \left(\frac{f}{\langle f \rangle}\right)^{-3} & \text{if } f \geq \langle f \rangle, \end{cases} \tag{12}$$

where $\frac{3}{2}N_0$ is the sample size and $\langle f \rangle$ is the mean value of f.

The Kinsey data showed that sexual preference is independent of sexual-outlet frequency. That fact supports applying inverse cubic distributions to distinct sexual-preference groups, for example, to male homosexuals.

One may speculate that an inverse-cubic distribution of sexual-outlet frequency, $N \propto f^{-3}$, is a Darwinian barrier in behavior space produced by competition for a finite resource. If so, the distribution is not determined by a particular set of environmental or social influences but rather may be hard-wired into our genetic make-up. In any case, we find that both the distribution of sexual-outlet frequency among American males and the distribution of new-partner rate among a limited population of British homosexuals are described by inverse cubics. (That result suggests that an inverse cubic distribution of risk may also describe the heterosexual population.)

Sexual-Contact Frequency versus New-Partner Rate—Which Determines the Growth of AIDS? It has been argued that the high new-partner rate among homosexuals has been the primary risk factor governing the growth of AIDS. Here we point out that if infectiousness is low, $i \ll 1$, then sexual-contact frequency rather than new-partner rate is the determining risk factor, provided the new-partner rate is greater than zero. First we note that an infected individual must infect *on the average* just one previously uninfected individual within the doubling time to produce a doubling of the number of cases. Since the doubling time of the infection has always been long compared to the new-partner exchange time (the current doubling time of the infection is more than 2 years), it is difficult to see how new-partner rate per se can be the primary risk factor. More partners and fewer sexual contacts per partner within the doubling time should transfer infection at the same rate as fewer (but some) new partners and more sexual contacts per partner. The most likely case is that new-partner rate and sexual-contact frequency are strongly correlated, but the available data are inadequate to confirm that hypothesis.

The observed correlation between high new-partner rate and infection could also be explained by the existence of a short period (several days to a week) of very high infectiousness (≈ 1) soon after initial infection followed by a long period (about 2 years) of low infectiousness. During a highly infectious period of such short duration, a victim of transfusion-related AIDS is not likely to infect his or her partner, but a homosexual with a high new-partner rate is. Thus a short spike of very high infectiousness is consistent with the high initial growth rate of AIDS (a doubling time of less than 6 months) observed among high-risk homosexuals and intravenous-drug users and with the long time (an average of more than 3 years) required for transfusion-infected people to infect their spouses.

Later we will discuss the role that a variability in infectiousness from person to person might play in the question of whether new-partner rate or sexual-contact frequency governs the growth rate of the epidemic. In any case, whichever is the causative risk, both can be described by an inverse cubic distribution, provided we

assume infectiousness is not correlated with risk behavior. Thus we assume the following distribution of risk behavior:

$$\frac{N(r)}{N_0} = \begin{cases} 1 & \text{for } r < 1 \\ r^{-3} & \text{for } r \geq 1, \end{cases} \tag{13}$$

where r is normalized so that a value of 1 is assigned to the mean value of r and $\frac{3}{2}N_0$ is the size of the population.

The Saturation Wave

We are now in a position to describe how the infection travels through the population. We start with our assumption of biased mixing, namely, that the population is divided into groups of individuals with similar risk behavior and that the members of each group interact primarily among themselves (intragroup preference). Since the relative growth rate of the infection is proportional to the risk behavior r, the time for the epidemic to approach saturation within each group will be proportional to r^{-1}. Also, higher-risk groups have fewer members than lower-risk groups, so higher-risk groups saturate much faster than lower-risk groups. Thus, after a member of the highest risk group is infected, that group quickly saturates, then the next lower group saturates, and so on. We say that a "saturation" wave of infection travels from high- to low-risk groups.

SATURATION WAVE PRODUCED BY BIASED MIXING

Fig. 7a. When the mixing among a population is biased (that is, when individuals with similar risk behavior (here new-partner rate) interact primarily among themselves), our model predicts the distributions by risk behavior of the number infected shown on the right. The distributions were calculated for various times t after an individual with very high risk behavior became infected. Note that the number infected approaches saturation first in the highest-risk group and then, as time passes, in successively lower and lower risk groups. We describe that situation by saying that a wave of saturation travels from high- to low-risk groups. Also shown (dashed line) is the initial distribution by risk $N(r)$ of the population, which is assumed to be an inverse cubic distribution.

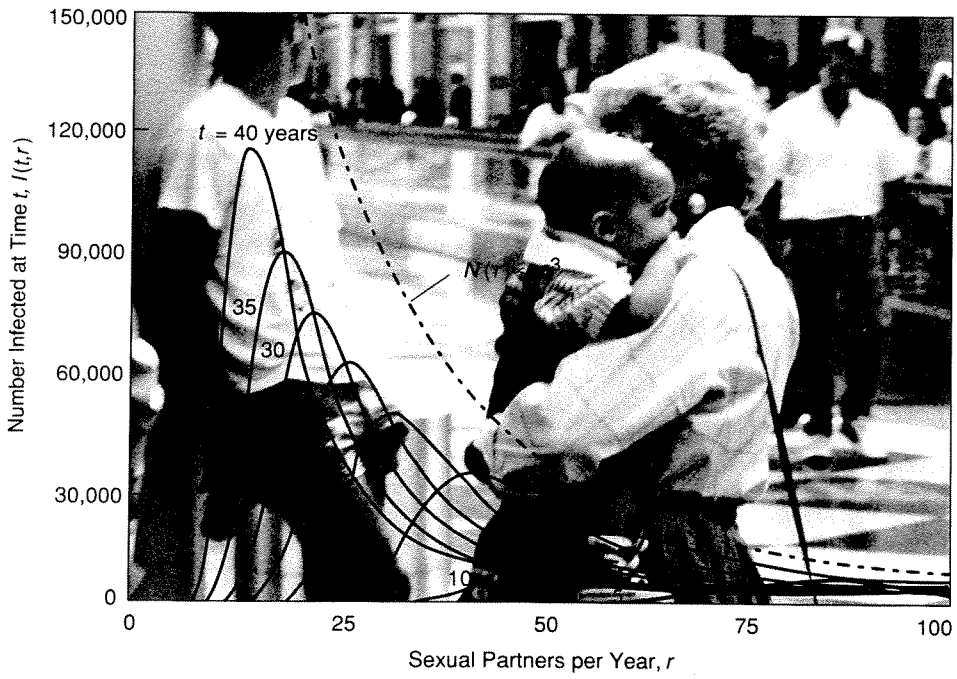


Figure 7a shows "snapshots" of the saturation wave of infection at successive times, calculated numerically from our general model. Note that the calculation separates those who progress to AIDS and death from those who are infected but do not yet have AIDS. Consequently, the plots of number infected versus risk value in Fig. 7a are always below the dotted curve representing the original distribution of risk among the population.

As time progresses, the wavefront (the low-risk end of each curve) moves from right to left, that is, from higher to lower risk values. At any given time all groups with risk values to the right of the wavefront are saturated, and all groups with risk

values to the left of the front have just a few infected members. It is primarily within the group composing the wavefront that the multiplication is taking place, and therefore the doubling time of the epidemic at any given time is primarily the doubling time of that group. Since within that active group the mixing is homogeneous, the number of infected within the group is growing exponentially, and, on average, each infected individual infects only one person within the group's doubling time.

The general model used to calculate the wave in Fig. 7a allows a small amount of mixing between groups. In addition, we allow for the possibility that some individuals were "seeded," or infected, before the start of the saturation wave. Therefore, the numbers of infected in all groups with risk values to the left of the wavefront are also growing exponentially, but at a relatively slow rate, and all groups with higher risk values are saturated, exhibiting no further growth in numbers of infected. Only the total number of infected individuals (the sum of the infected in all groups) is growing as a power law.

Fig. 7b shows what happens when we assume homogeneous rather than biased mixing. Note that the saturation wave moving from high- to low-risk groups disappears. Instead, the number infected in the average-risk group is always larger than the number infected in high-risk groups. Thus homogeneous mixing contradicts the finding of the CDC that most early victims of AIDS were high-risk individuals. Moreover, homogeneous mixing yields exponential rather than power-law growth.

NO SATURATION WAVE WITH HOMOGENEOUS MIXING

Fig. 7b. When the mixing among a population is homogeneous rather than biased, the saturation wave in Fig. 7a disappears. Instead the maxima in the distributions of number infected always occur in low-risk groups, even early in the epidemic. Such a situation is contrary to the findings of the Centers for Disease Control.

Calculation of the Saturation Wave. We will now make the above qualitative description of the saturation wave into a quantitative model. For simplicity we ignore intergroup mixing and calculate the wave of infection as if each risk group grows independently to saturation. However, such a simplistic calculation yields essentially the same results as the more complete model that includes a small amount of mixing between groups (see "Numerical Results of the Risk-Based Model of AIDS").

Once the saturation wave starts, the total number of infected I at any given time is roughly the sum of all individuals from the highest-risk individual down to individuals with risk behavior r_*, the value of r at the front of the saturation wave. Thus the number of infected is equal to the integral of all individuals with $r \geq r_*$:

$$I(r_*) = \int_{r_*}^{\infty} N(r)dr = \frac{1}{2}N_0 r_*^{-2}, \tag{14}$$

where r_* is the risk behavior of the lowest risk group in which most members are infected and $N(r)$ is the number of individuals with risk behavior r, as defined in Eq. 13.

We will now convert Eq. 14 into an equation for the number of infected as a function of time. We do this by calculating the time required to saturate the group of $N(r_*)$ individuals at the front of the wave. We assume all risk groups are seeded before the start of the saturation wave at $t_* = 0$. Within each risk group the mixing is homogeneous, so the number infected with risk behavior r_* grows exponentially, or as $I(0, r_*)e^{\alpha' r_* t_*}$, where $I(0, r_*)$ is the number infected with risk behavior r_* at $t_* = 0$. Although the relative growth rate decreases as the group approaches saturation, we neglect this slowing down and say that exponential growth continues until the number infected is approximately equal to the total number in the group. (We also ignore the slow depletion of number infected by death.) Thus

$$N(r_*) \approx I(0, r_*)e^{\alpha' r_* t_*}. \tag{15}$$

Then t_* is the time to saturate the group with risk behavior r_*. Solving Eq. 15 for t_* gives

$$t_* \approx \frac{1}{\alpha' r_*} \ln\left(\frac{N(r_*)}{I(0, r_*)}\right). \tag{16}$$

To the accuracy of this model, we will consider the fraction of each group initially infected, $N(r_*)/I(0, r_*)$, to be slowly varying. Then Eq. 16 says that the time t_* to saturate a group with risk r_* is proportional to $1/r_*$.

We can now express Eq. 14 in terms of t_* by replacing r_* with a constant times $1/t_*$. Thus we determine that the dominant time-dependent behavior of the number infected is

$$I(t_*) \approx I_1 t_*^2,$$

where the value of I_1 is not yet determined. We have assumed that some individuals were seeded, or infected, before a member of the highest-risk group started the saturation wave, so we add an unknown constant I_0 to obtain

$$I(t_*) \approx I_0 + I_1 t_*^2. \tag{17}$$

Although Eq. 17 cannot be valid at $t_* = 0$ (it implies that $\frac{dI}{dt_*} = 0$ at $t_* = 0$, which does not make sense), we will not attempt to refine it but instead lump all the uncertainties about the very early growth in the constant I_0. Thus we say that after the start of the saturation wave at $t_* = 0$, the number infected grows as the square of time. Since in our model the quadratic growth term $I_1 t_*^2$ will be associated with the cubic growth of AIDS, the unknown number of additional infected persons I_0 will be associated with deviations from purely cubic growth of AIDS before 1982.5.

The Progression to AIDS from Infection. Given the number infected as a function of time, we now need to estimate the resulting growth in the number of AIDS cases. The most extensive data on the conversion from HIV infection to AIDS have their origin in a study by the San Francisco Department of Health on the spread of hepatitis B among a group of homosexual men. That study took place between 1978 and 1982 and was extended in 1984 to track HIV infection. A subset of the original group continues to be monitored for clinical evidence of AIDS. The blood samples from that study have been an invaluable source for determining the time lapse be-

PROBABILITY OF DEVELOPING AIDS

Fig. 8. The cumulative probability of developing AIDS at time τ after infection $C(\tau)$ versus τ. The time of infection is assumed to be the time at which antibodies to HIV are first detected in the blood. The data were supplied by the San Francisco Department of Health. $C(\tau)$ is near zero for the first two years after infection and then increases appoximately linearly at a rate of 0.06 per year. Linear extrapolation of the data at that constant rate (dashed line) indicates that $C(\tau) = 0.5$ at 10 years after infection and $C(\tau) = 1$ at 18 years after infection. Recent data extending to 10 years after infection agree with that extrapolation.

tween infection with HIV and the onset of AIDS.

Let $C(\tau)$ be the cumulative probability of conversion to AIDS at τ years after infection. Figure 8 is a graph of $C(\tau)$ versus τ derived from the San Francisco study for $\tau \leq 8$ years. For the first two years after infection, $C(\tau)$ is nearly zero. Then it increases almost linearly at a rate of 0.06 per year. Newly gathered data extend the steady rise to 10 years after infection.

The apparently inexorable increase in $C(\tau)$ is consistent with the steady decline, with time since infection, in the number of T4 lymphocytes in the blood of infected persons. Those so-called T4 helper cells are central players in the functioning of the immune system, and their demise results in a progressively decreasing ability of the immune system to destroy invading pathogens. Moreover, the rate of T4 cell destruction found in an infected person is correlated with the time required for that person to convert to AIDS. These facts suggest that HIV infection always proceeds to AIDS, as does a study by Bordt et al. of infected individuals in Frankfurt, East Germany. More than 90 per cent of that study group progressed from one stage of immune destruction to the next. The Frankfurt data indicate that at least 90 per cent of those infected will develop AIDS. Thus, even though the San Francisco study covers only 10 years of experience, we argue that a reasonable extrapolation of the data is to assume a constant rate of change in cumulative conversion probability of 0.06 per year starting 2 years after infection. In other words, we assume that

$$\frac{dC(\tau)}{d\tau} = \begin{cases} 0 & \text{for } 0 \leq \tau \leq 2 \\ 0.06 & \text{per year for } 2 < \tau < 18 \\ 0 & \text{for } \tau \geq 18. \end{cases} \tag{18}$$

Equation 18 implies that the cumulative probability of converting to AIDS is 50 per cent at 10 years after infection and 100 per cent at 18 years after infection.

Because conversion to AIDS has a nonzero probability of happening at any time between 2 to 18 years after infection, the growth rate in the number of AIDS cases, $dA(t)/dt$, at any given t is the sum over past times τ of the product of the growth rate of newly infected at $t - \tau$ years, $dI(t - \tau)/dt$, and the differential probability

of conversion to AIDS at τ years since infection (or at time t), which is $dC(\tau)/d\tau$. That complicated sum is written as a convolution integral over past times τ:

$$\frac{dA(t)}{dt} = \int_0^\infty \frac{dI(t-\tau)}{dt}\frac{dC(\tau)}{d\tau}d\tau. \tag{19}$$

Using Eq. 18, we reduce Eq. 19 to

$$\frac{dA(t)}{dt} = 0.06\int_2^{18}\frac{dI(t-\tau)}{dt}d\tau, = 0.06[I(t-2) - I(t-18)] \text{ for } t \leq 18 \text{ years.} \tag{20}$$

Replacing $I(t-2)$ with Eq. 17, neglecting $I(t-18)$ because it is small, and evaluating $\frac{dA}{dt}$ from Eq. 2, we obtain

$$3A_1t^2 = 0.06[I_1(t_* - 2)^2 + I_0] \text{ for } t > 1.3 \text{ years.} \tag{21}$$

Thus we see that if

$$I_1 = \frac{3A_1}{0.06} \approx 8700, \tag{22}$$

$$t_* = t + 2, \tag{23}$$

and if I_0 is small compared to $(1.3)^2I_1 \approx 15,000$, then our model fits very closely the AIDS case data in Eqs. 1 and 2. The time shift of 2 years reflects our approximation that AIDS does not develop during the first two years following infection.

Equation 17 for the number of infected becomes

$$I(t) = 8700(t+2)^2 + I_0, \tag{24}$$

where t is the time since 1981.2. This equation will be valid from the start of the saturation wave, which occurs before $t = 1.3 - 2$ years $= -0.7$ years (1980.5). Hence we estimate that in 1988.2, or $t = 7$ years, the number of infected persons that will eventually be reported as CDC-defined AIDS cases (using the pre-1987.5 definition) was

$$I \approx 8700(9)^2 \approx 700,000. \tag{25}$$

To summarize, our biased-mixing, risk-based model shows a cubic growth of AIDS independent of learning and predicts that the infected population initially grew as the square of time. Both the number infected and the number of AIDS cases have doubling times that increase linearly with time. We have associated the cubic growth in AIDS cases with a quadratic growth in infections, which is produced by a saturation wave moving from high- to low-risk groups. We have not discussed what happens prior to the start of the saturation wave, since that is more speculative. However, in "The Seeding Wave" we present a plausible scenario for the initial spreading of infection.

Consequences of the Model

We use the simple model described above to answer a number of questions. These questions are also relevant to our general model and to other more complex models still to be developed.

Present Number Infected. The estimate of about 700,000 infected in 1988.2 is significantly less than the estimate of 1.5 million made several years ago but agrees more closely with the CDC estimates of 1 to 1.5 million. While the earlier num-

ber was probably an overestimate, the estimate obtained from Eq. 24 was not corrected for cases not reported, which amount to about 10 per cent of the total, and for cases falling outside the pre-1987 CDC definition, which amount to about 20 per cent of the total. The estimate of 700,000 must therefore be multiplied by a factor of $1/(0.9 \times 0.8) = 1.4$. Thus our model predicts that approximately 1 million individuals in the United States were infected with HIV by 1988.2. This prediction is based on the assumption that behavioral changes due to learning did not greatly reduce the growth of infection. If learning has been effective, the number infected could be less. More likely, however, is that infectiousness depends on the stage of the disease, which, in turn, implies a greater number infected (see below).

Average Time Since Infection. To determine whether behavioral changes could have affected the growth of AIDS, we must first determine how long ago, on average, those persons now developing AIDS were infected and then question whether learning was a significant factor at that time. The mean time since infection $\bar{t}$ of the AIDS cases at time t is given by

$$\bar{t} = \frac{\int_0^\infty \frac{dI(t_*-\tau)}{dt_*}\tau\frac{dC(\tau)}{d\tau}d\tau}{\int_0^\infty \frac{dI(t_*-\tau)}{dt_*}\frac{dC(\tau)}{d\tau}d\tau} = \frac{1}{3}\frac{t_*^3 - 12t_* + 16}{(t_*-2)^2} \approx \frac{1}{3}t + 2 \text{ years.} \qquad (26)$$

For 1988.2, $t = 7$ years and $\bar{t} \approx 4.3$ years. That is, those persons developing AIDS in 1988.2 became infected, on average, in 1983.9. One might expect the mean time since infection to be closer to 10 years, the time when the cumulative probability for conversion to AIDS $C(\tau)$ equals 0.5. The mean time is much shorter than 10 years because the fast growth rate of the infected population relative to the slow rate of conversion to AIDS biases the time since infection of the AIDS cases in 1988.2 closer to the time when most were infected.

Learning and Decreasing Growth Rate. We emphasize that 1983.9 is just about when learning started on a large scale, that is, when the bath houses in San Francisco were closed and safer sex practices began to be accepted. Therefore, we may expect that a decrease in the growth of AIDS among homosexual men below the cubic growth has already started. The change in the definition of AIDS makes that difficult to see in the data. Our estimate of the number infected in 1988.2 is based on extrapolating the observed initial cubic growth of AIDS cases into the future, so the actual number infected in 1988.2 may have been considerably less than a million due to learning. In any case the decreasing relative growth rate observed until early 1988 cannot be ascribed to learning.

Risk Behavior As a Function of Time. Our model suggests that individuals with the highest risk behavior are infected first and that, as time goes on, individuals with lower risk behavior become infected. We can quantify that change over time provided we have estimates of the population size and the present number infected.

We consider one sector of the population, namely, the 40 million males between the ages of 20 and 40 residing in principal American cities, and limit the group to those who actively exhibit homosexual behavior. If the Kinsey estimate for the percentage still holds, 10 per cent of the 40 million males, or 4 million, are homosexual. Equation 13 tells us that the size of the population is $\frac{3}{2}N_0$, so for the population being considered here, $N_0 = 2.7$ million. From Fig. 3 we learn that 65 per cent of the AIDS victims are homosexuals so we can equate I from Eq. 14 to $0.65I$ from Eq. 24. Neglecting I_0 we have

$$\frac{1}{2}N_0 r_*^{-2} = (0.65)8700(t+2)^2. \qquad (27)$$

Substituting the value of 2.7 million for N_0 and solving Eq. 27 for r_*, we find that the risk behavior of the male-homosexual group being infected at time t varies inversely with time:

$$r_* = \left(\frac{2,700,000}{(2)(0.65)(8700)}\right)^{1/2}(t+2)^{-1} \approx 15(t+2)^{-1}. \quad (28)$$

Recall that r and r_* were normalized so that they are multiples of the average risk behavior and t is the time since 1981.2.

Thus, our model suggests, for example, that most homosexual victims of AIDS in 1988.2 were infected 4.3 years earlier when t = 2.7 years, that 200,000 were infected at that time, and that their risk behavior then was about 3 times the average behavior. More generally the model predicts that the risk behavior of those being infected is a continuously decreasing function of time and that the earliest infected, who in general were the earliest victims of AIDS, were those with the highest risk behavior. That last point coincides with the original findings of the CDC and others. In contrast, models based on homogeneous mixing (recall Fig. 7b) do not predict this time-dependent behavior, since at any time most of those being infected are members of the average- and not the higher-risk groups. The high average risk behavior at time of infection characteristic of the early cases of AIDS is a strong argument for the importance of including behavior in any model of the AIDS epidemic.

Mean Probability of Infection. We can combine results for the risk behavior as a function of time and the growth of the number infected as a function of time to estimate $\bar{i}$, the mean infectiousness, or mean probability of transferring infection per sexual contact. For example, let's consider those developing AIDS in 1988.2, who had, on average, a new-partner rate of approximately 3 times the mean.

Now suppose sexual-contact frequency is correlated with new-partner rate; that is, suppose a new-partner rate of 3 times the mean implies a sexual-contact frequency of 3 times the mean. Three times the mean sexual outlet frequency f is 450 sexual outlets per year (see Fig. 6), the major fraction of which can, according to Kinsey et al., be considered possible infectious contacts. Neglecting I_0 in Eq. 24, the relative growth rate of the infection α is given by:

$$\alpha \equiv \frac{dI/dt}{I} = \frac{2}{t+2}. \quad (29)$$

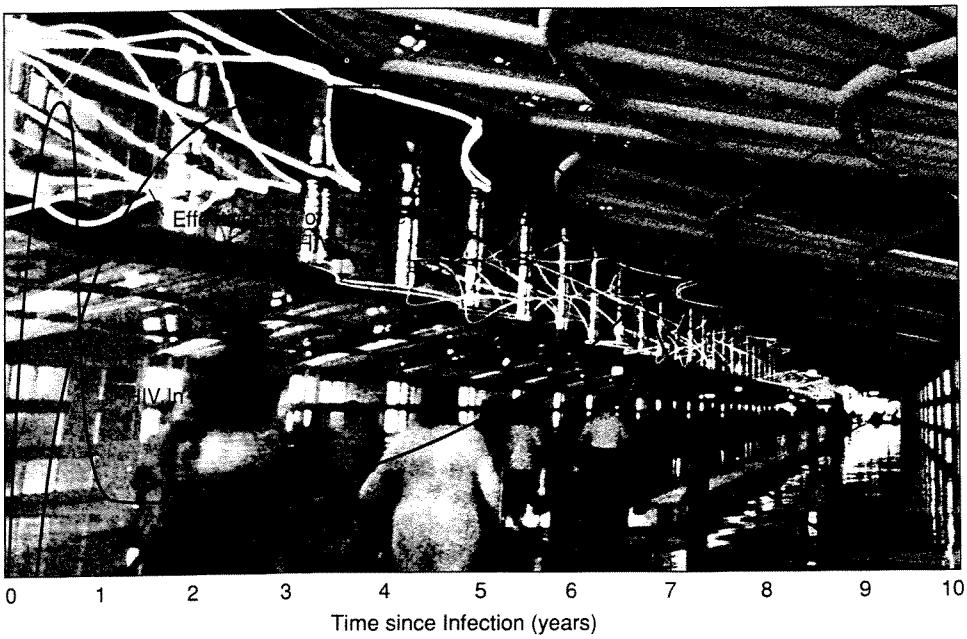
Thus at t = 2.7 years, α = 0.43 per year. Because the growth is primarily within the risk group at the front of the saturation wave, and the growth within that group is exponential, the doubling time is given by $t_d = (\ln 2/\alpha)$ = 1.6 years. On the average, each infected member of the group infects only one new partner per doubling time. Thus the average infected person has $f t_d$ = (450)(1.6) = 720 sexual contacts and infects one previously uninfected person. In other words, $720\bar{i}$ = 1 and the mean infectiousness is approximately 0.0014. If the sexual-contact frequency is uncorrelated with new-partner rate, then we assume the sexual-contact frequency is the mean value, or 150 sexual outlets per year, and the mean infectiousness must be three times larger or about 0.004. These estimates are on the low end of the estimates of 0.003 to 0.1 made by Grant, Wiley, and Winkelstein. Also, the large uncertainties in our estimates are proportional to the uncertainties in dI/dt in 1983.9 and the uncertainties in f.

Time-Dependent Infectivity. Our estimates for the mean infectiousness (or infectivity) say nothing about the extreme variability observed from one individual to another. In an extraordinary example, four out of eight Australian women were infected with HIV from one donor sample of cryo-preserved semen split ten ways.

By contrast, in New York ninety artificial inseminations with infected semen gave rise to no infections. Is the variability due to episodic infectivity in individuals or to different strains of virus? If the Australian example were due to a particularly virulent strain of virus, several hundred times more infectious than the average, then that strain would have rapidly eclipsed all others and the growth of infection would have been many times faster since the Australian incident in 1982. Since that clearly has not happened, we must consider other possible causes of the large variability in infectivity: (1) a few individuals may be highly infectious for a period longer than the doubling time; (2) all individuals may be highly infectious for very short episodes of time; (3) highly infectious mutations may quickly mutate to less infectious ones; or (4) some individuals may be more infectious than others. Dr. G. J. Stewart has suggested that his Australian donor was in the active pre-mononucleosis-like phase of infection, which occurs before the debilitating lymphoma characteristic of pre-AIDS patients, and was therefore highly infectious. Stewart also cites three instances of infected women who have not yet (in 6 years) infected their unprotected male partners. On the other hand the very rapid spread of infection in the Kagera region of Tanzania (from only a few seropositive persons in 1984 to 43 per cent of urban adults in 1988) may indicate that a more virulent strain has emerged.

Our model tacitly assumed a constant infectivity per unit time so that the relative growth rate α was proportional to risk behavior. However data from Walter Reed Army Medical Center and other institutions suggest that the amount of virus in the blood, and therefore the infectiousness, follows the curve shown in Fig. 9. Further studies are desperately needed to pin down the course of AIDS within individuals and the resulting infectivity as a function of time, but for the moment the data shown in Fig. 9 are the best estimate we have. Those data indicate that for a brief period following infection, people are highly infectious, then for several years the immune response is able to halt viral replication, thereby reducing infectiousness to a very low level, and finally, as the immune system deteriorates and the T4 cell count declines, infectiousness rises steadily. If this pattern is correct, how does it alter the predictions of our risk-based model?

We mentioned earlier that a short period (several days to several weeks) of high infectiousness (greater than 0.5) immediately after infection could have driven the early phase of the epidemic, when new-partner rates were greater than one new part-



HIV REPLICATION AND INFECTIVITY

Fig. 9. Dependence of infectivity on time since infection most likely follows the red curve, which describes the amount of HIV in the body. Initially the virus replicates rapidly, but then the immune system mounts its defense and viral replication is stopped. At about 2 years after infection, the immune system begins to break down and viral replication resumes. The black curve depicts the effectiveness of the immune response to HIV. (The figure was adapted, with permission of Scientific American, Inc., from one appearing in the article "HIV infection: The clinical picture" by Robert R. Redfield and Donald S. Burke. *Scientific American*, October 1988.)

ner per week. A spike of high infectiousness of that duration is consistent with the observed cubic growth in the high-risk population provided it is followed by a period of low infectiousness lasting roughly several years. Further, if infectivity is correlated with decreasing T4 cell count and therefore begins rising a few years after initial infection, our model predicts a growth in AIDS cases proportional to a power of time greater than 3. Thus we expect a transition in the growth pattern of the epidemic as the saturation wave moves from groups with high new-partner rates to those with lower ones. This change would reflect the fact that among the high-risk population, the disease spreads most during the short, initial infectious period, whereas, among the low-risk population, the disease spreads most during the five to ten years of increasing infectivity in the later stages of disease. Since the heterosexual population is characterized by relatively low new-partner rates, the latter mode of growth will probably dominate in that group. (The effects of time-dependent infectivity for the more complete model are presented in "Numerical Results of the Risk-Based Model.")

Do Super Spreaders Exist? We have already pointed out that the low average infectiousness implies that sexual-contact frequency rather than new-partner rate determines the growth rate of the epidemic. However, the new-partner rate within a group can be the dominating risk factor if a small percentage of individuals within the group are highly infectious. If such individuals have more new partners but maintain the same sexual-contact frequency, they will infect more individuals. Since super spreaders infect almost every one of their partners, the fraction of such highly infectious individuals must be small to maintain the observed growth rate. The singular Australian case supports that possibility. Therefore, an understanding of the biological mechanism of high infectivity and means for identifying highly infectious individuals become important to controlling the epidemic.

High-Risk Heterosexual Groups. If a self-sustaining epidemic exists among heterosexuals, then our model suggests that it would first occur among nonmonogamous heterosexuals whose sexual-contact frequency and/or new-partner rate were several times the mean of that group or higher. At this time, a firm determination can be made only by choosing a large enough sample of those high-risk individuals and determining that more of them are infected than can by explained by unwitting contacts with homosexuals and intravenous-drug users. The experience of interviewers has shown that many people who initially claim only heterosexual risk may not be telling the truth. This creates a bias among researchers that anyone denying other risks is either lying or mistaken (for example, female contacts of intravenous-drug users may be ignorant of their partner's drug habit).

Masters, Johnson, and Kolodny have made an attempt to choose a high-risk, purely heterosexual sample by selecting heterosexuals who had more than 5 new partners per year for 5 years running. (They estimate that less than 5 per cent of the nonmonogamous, sexually active heterosexual population satisfy that criterion.) They found that 6 per cent of that group was infected. Their study has been severely criticized on methodological grounds. Although we are not in a position to defend the details of the study, we do believe that their philosophy was correct: the only way to make an early estimate of the spread of AIDS among heterosexuals is to look at the high-risk end of that population. Without such studies the disease may spread silently as behavior goes unchanged among a population that believes it is not at risk.

Conclusions

We have constructed a risk-based, biased-mixing model that reproduces the observed cubic growth of AIDS when: the risk behavior, quantified as r, is distributed

among the population as r^{-3}; either new-partner rate or sexual-contact frequency dominates the risk behavior or both are positively correlated; and the cumulative probability of conversion to AIDS increases at an approximately constant rate. The implications predicted by or consistent with the model are many. In the hope that those implications will inspire further research and promote greater awareness of the threat of AIDS, we end by listing them.

- The total number of persons infected with HIV in 1988 was roughly one million.

- The mean time between infection and onset of AIDS is an increasing function of time.

- The decreasing relative growth rate of AIDS cases observed through 1988 was not due to changes in behavior.

- The mean risk behavior of AIDS victims at time of infection is a decreasing function of time.

- The mean probability of infection per sexual contact may be as small as 0.004 to 0.001.

- A slow increase in infectivity during the progression from infection to AIDS could change the growth of AIDS from the cubic growth rate now observed to something faster, and behavior modification could change it to something lower.

- New-partner rate is the dominant risk factor if sexual-contact frequency and new-partner rate are strongly correlated or if a few per cent of the population have a very high infectiousness; otherwise sexual-contact frequency is the dominant factor.

- Most major subpopulations, both demographic and geographic, were infected by a few high-risk individuals early in the epidemic, and only small, highly socially isolated groups may remain untouched by the epidemic.

- One likely path by which the infection initially reached the high-risk groups was by an initial seeding of the average-risk population (see "The Seeding Wave"). A seeding wave then progressed from low- to high-risk groups before 1979. Simulation of such a seeding wave suggests that the first case of infection could have occurred in the average population in the late 1960s. Only somewhat less probable is occurrence of the first case of AIDS in the higher-risk groups in the late 1970s.

- After the highest-risk group is saturated (most of its members are infected), a saturation wave of infection proceeds to lower-risk groups, producing the cubic growth in AIDS cases.

- Growth of AIDS cases within the purely heterosexual, drug-free population may also be governed by a power law (most likely cubic). However only by measuring prevalence in high-risk heterosexual groups adequately isolated from other known risk groups can such a determination be made.

- More speculative is the implication that the initial spike of the time-dependent infectivity caused the initial rapid growth in the homosexual and intravenous-drug-using populations and that the gradual increase in infectivity about two years following infection may be driving a second much slower epidemic (measured in decades) among the heterosexual drug-free population. That latter mode of slow spread may be the strategy evolved by the virus to survive in equilibrium with its human hosts.

Our risk-based model is seen by many as controversial. Certainly data on sexual behavior and mixing patterns that firmly substantiate our assumptions are sadly lacking in the literature. Even more unfortunate is the difficulty in collecting data on private behavior. The singular dedication of Kinsey must be emulated on a larger de-

mographic scale with a societal consensus of the necessity for truthful answers and the guarantee of legal protection. Such data may take many years to collect, whereas urgency is needed to help us stem the spread of this deadly disease. Thus we have used the available data to develop what we feel is a likely and plausible model for the growth of the epidemic. Whether exactly right or not, the model raises questions that we cannot ignore. It also offers simple quantitative tools to estimate the size of the problem and to quantify the effectiveness of strategies aimed at minimizing the growing threat. ■

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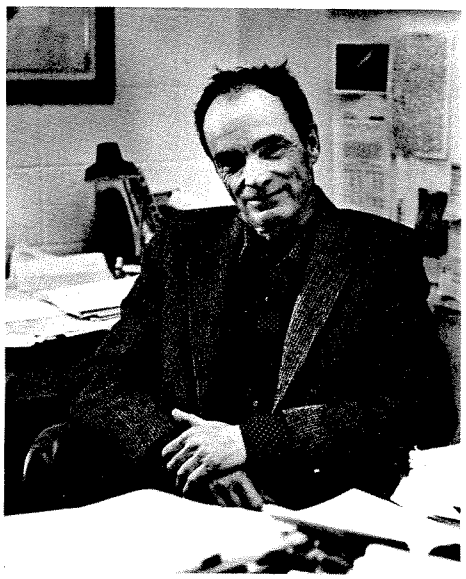

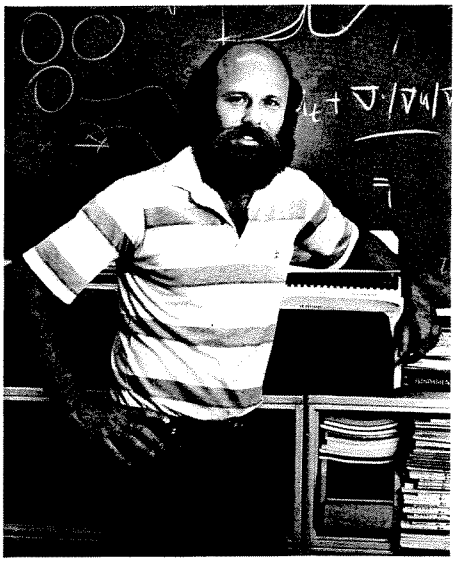

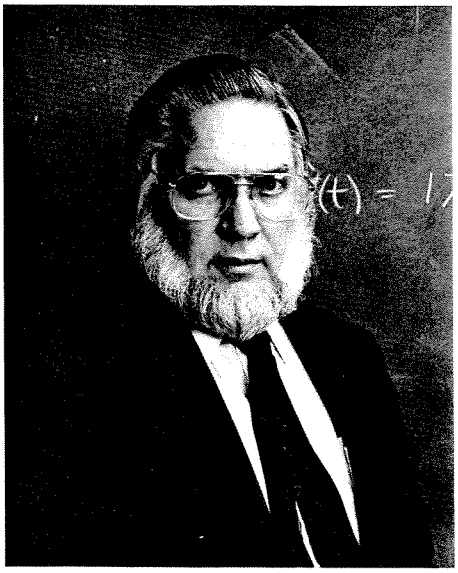

James M. Hyman is currently the Administrative Manager for the Advanced Computing Facility at Los Alamos. Before coming here in 1976, he was an instructor and research assistant at the Courant Institute of Mathematical Sciences. He received his M.S. (1974) and Ph.D. (1976) degrees in mathematics from the Courant Institute and two B.S. degrees, one in physics and the other in mathematics, both with honors, from Tulane University in 1972. His research interests include the development and analysis of numerical methods and software for the solution of partial differential equations. One goal of this work is to develop expert systems that automatically generate a computer code approximating the solution to mathematical models for, say, oil flow in a reservoir, laser fusion, or the weather. Recently his interest has turned toward mathematical models for understanding and predicting the AIDS epidemic.

E. Ann Stanley came to Los Alamos in 1984 as a postdoctoral fellow and became a staff member in the Mathematical Modeling and Analysis group in the Theoretical Division in 1987. She received a Ph.D. in applied mathematics from the California Institute of Technology in 1985 and a B.S. in engineering mathematics from the University of California in 1979. For her thesis she developed and analyzed mathematical models for Case II diffusion, the phenomenon in which a glassy polymer absorbs a fluid, a sharp front forms between the wet and dry regions, and the front moves forward at a speed proportional to time. After coming to Los Alamos, she continued working on this and other nonlinear diffusion problems. She became involved in the AIDS research partly because of previous work on a model of the diffusion of fox rabies across Europe. She enjoys playing the flute, taking modern dance classes, bicycling, skiing, and other outdoor activities.

Clifford R. Qualls is a professor of statistics at the University of New Mexico. He received a B.A. from California State College in 1961, an M.A. from University of California in 1964, and his Ph.D. from the University of California in 1967. His research interests include applied statistics, biostatistics, stochastic processes, and time series, and he supervises a computer center for the Department of Medicine at the University. He has been a visiting staff member at Los Alamos since 1975, working on statistical studies of neutral particle beams as well as the AIDS epidemic. He is currently President of the Albuquerque chapter of the American Statistical Association.

Scott P. Layne (see the biography following "The Kinetics of HIV Infectivity").